REMARKS

Claims 1-9, 11-18, 20-28, and 39-44 are pending. Claim 20 is "currently amended" to add the word "less," which was inadvertently deleted in the amendment filed June 1, 2010. Claims 1, 20 and 24 have also been amended to require that the producing step be completed in 2 hours. Claims 39, 41 and 43 have been canceled. Support for the amendments can be found at least at page 4 in the last paragraph. No new matter has been added.

35 U.S.C. § 103

Ladner, Anderson, and Chandrashekar. The Office at pages 2-9 of the Action maintains the position that claims 1-9, 13, 15-17, 20-27, and 39-44 are allegedly obvious in light of Ladner *et al.* (U.S. Pat. No. 5,403,484), Anderson (U.S. Pat. No. 6,649,419), and Chandrashekar *et al.* (U.S. Patent No. 5,854,051).

Applicants respectfully traverse this rejection.

Ladner *et al.* discloses a method for screening a library of diverse phage, each displaying heterologous protease inhibitors having binding affinity for a target immobilized on a solid substrate. Ladner *et al.* teaches that the phage bind to the support through the target, the phage that do not bind the target are eluted away, the particle-bound phage are infected into cells, and the phage are replicated from the cells in the presence of the target immobilized to the support. See, *e.g.*, column 142, line 14, through column 144, line 36.

Anderson teaches a method of using magnetic beads to isolate biological components of interest, where the component of interest binds to a target that is attached to the bead. See, *e.g.*, column 11, lines 29-37.

Chandrashekar *et al.* discloses protein expression from a phage cDNA library by incubating the library for four hours on *E. coli* XL1-Blue plates, and then expressing the protein by laying IPTG filters over the plates for 3 hours. The filters are then washed and

screened with an antibody to identify plaques expressing the protein of interest (a five hour procedure). See, *e.g.,* paragraph spanning columns 28-29. Chandrashekar *et al.* does not teach or suggest a method that would provide a second round of selection in a single day.

There is no teaching or suggestion in any of the three references, alone or in combination, that the producing step could be performed in less than 2 hours. As stated in the Ladner Declaration submitted September 22, 2009, Applicants discovered a more rapid method for screening binding peptides by phage display. Applicants discovered, *inter alia*, that target-specific phage can be used to infect bacteria, even when in the presence of target. No elution step is required. Further, no phage preparation or pooling step is needed after phage-infected bacteria are cultured. Of particular significance, Applicants have discovered that large quantities of phage from a given round of selection do not need to be prepared prior to initiating a subsequent round of selection. As a result, dramatically reduced incubation times can be employed after bacteria are infected with phage. Indeed, not only can the cultures be incubated for less than 4 hours, but even times of less than 2 hours or 1 hour can be sufficient. See the Ladner Declaration at page 6.

The art cited by the Office would not lead one of ordinary skill in the art to the conclusion that the step of phage amplification could be carried out in less than **two** hours. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claims 1-9, 13, 15-17, 20-27, and 39-44 as being obvious in view of Ladner *et al.*, Anderson, and Chandrashekar *et al.*

Ladner, Anderson, Chandrashekar, and Janda. At pages 9-10, the Office maintains that claims 1-9, 12-17, 20-28, and 39-44 are obvious in light of Ladner *et al.,* Anderson, Chandrashakar *et al.*, and Janda (U.S. Pat. No. 5,571,681).

The disclosures of Ladner *et al.*, Anderson, and Chandrashekar *et al.* are described above.

Janda discloses phagemid display for screening combinatorial libraries, and that combinatorial libraries can include covalent conjugates that are immobilized by attachment to a substrate through a solid phase. Janda discloses a selection method that involved applying a phage library to wells of a microtitre plate and allowing phage to bind to a substrate attached to the wells. Non-adherent phage were washed away and then covalently phage are eluted, infected into *E. coli* XL1-Blue cells, and amplified over the course of four hours. Kanamycin was then added and the culture incubated overnight to further amplify the cells. Phage preparation and further panning/affinity selections were repeated. See column 25, lines 15-50.

At page 10 of the Office Action, the Office states that:

> In describing the reactions for contact phage with the host cell, incubating the cell, and expressing the phage in the host cell, the processes can be carried out in less than four hours, such as the 15 minutes to infect the XL1-Blue cells, and the two hour culturing—note that the overnight cell selection with kanamycin is not required due to the beads being able to select the phage of interest and only captures progeny phage produced from the first round of binding to the bead that produced in the host cell (col. 25, lines 37-50).

Applicants disagree that one of ordinary skill in the art would read Janda *et al.* to suggest that the step of the overnight incubation, with or without, kanamycin could be skipped, even in view of the teachings of Ladner *et al.*, Anderson and Chandrashekar *et al.*

In Ladner *et al.*, phage that bound to target were used to infect bacterial cells, the phage-infected bacterial cells were incubated until plaques formed (12-18 hours), and then the plaques had to be pooled, before another round of selection with fresh target was initiated. In Janda, the eluted phage were used to infect bacterial cells, and the cultures were incubated for longer than overnight. The next day, the phage had to be prepared

from the overnight cultures and then another round of selection with fresh target could be initiated.

None of the references, alone or in combination disclose incubation of the phage for less than **two** hours, or that such a short incubation time would have been suitable. Applicants therefore request reconsideration and withdrawal of the rejection of claims 1-9, 12-17, 20-28, and 39-44 as being obvious in view of Ladner *et al.,* Anderson, Chandrashekar *et al.* and Janda.

Ladner, Anderson, Chandrashekar, and McCafferty. The Office at pages 10-12 maintains that claims 1-9, 13, 15-18, 20-27, and 39-44 are allegedly obvious in light of Ladner et al., Anderson, Chandrashekar *et al.*, and McCafferty *et al.* (U.S. Pat. No. 5,969,108; hereinafter "the '108 patent").

McCafferty *et al.* teaches the use of mutator strains for combinatorial chemistry when using phage.

None of the cited references, alone or in combination disclose incubation of the phage for less than **two** hours, or that such a short incubation time would have been suitable. Applicants therefore request reconsideration and withdrawal of the rejection of claims 1-9, 13, 15-18, 20-27, and 39-44 as obvious in light of Ladner *et al.*, Anderson, Chandrashekar *et al.*, and McCafferty *et al.*

Ladner, Anderson, Chandrashekar, Janda, and Steinbuchel. At pages 12-13 of the Action, the Office maintains that claims 1-9, 11-17, 20-28, and 39-44 are obvious in light of Ladner *et al.*, Anderson, Chandrashekar *et al.*, Janda, and Steinbuchel *et al.* (U.S. Pat. No. 6,022,729).

Steinbuchel *et al.* disclose the use of certain host cells, such as XL1-Blue™, for producing mutant polypeptide strains.

Again, none of the cited references, alone or in combination disclose incubation of the phage for less than **two** hours in a method for selecting phage that encode a target

binding protein, or that such a short incubation time would have been suitable. Applicants therefore request reconsideration and withdrawal of the rejection of claims 1-9, 11-17, 20-28, and 39-44 as obvious in view of Ladner *et al.*, Anderson, Chandrashekar *et al.*, Janda, and Steinbuchel *et al.*

CONCLUSION

Applicants submit that all of the pending claims are in condition for allowance, and notice to this effect is respectfully requested. Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor do Applicants concede that there are not other good reasons for patentability of the presented claims or other claims.

A Petition for Extension of Time for One Month is attached. The Commissioner is hereby authorized to apply the fee of $130, and any other necessary charges, or any credits, to Deposit Account No. 50/2762, referencing Attorney Docket No. D2033-701910.

Respectfully submitted,
Ladner et al., Applicants

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